61 CIGARETTE SMOKING INFLUENCES EICOSANOID PRODUCTION BY THE COLONIC MUCOSA IN A DOSE DEPENDENT MANNER

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Cigarette smoking is an important factor in the pathogenesis of inflammatory bowel disease (IBD), with smoking being positively associated with Crohn's disease (CD); and negatively associated with ulcerative colitis (UC), with the proposal that smoking protects against UC.

Inflammatory bowel disease is characterised by chronic and acute inflammation of the intestinal mucosa and submucosa, with resultant chronic diarrhoea. Investigation of the mediators responsible for perpetuating the inflammatory response have shown that eicosanoids, particularly prostaglandin E_2 (PGE_2) and leukotriene B_4 (LTB_4), are elevated, especially in the active phase of the disease. Cigarette smoking has been shown to inhibit PGE_2 synthesis by the gastric mucosa, while alveolar macrophages from smokers have reduced capacity to synthesis both PGE_2 and LTB_4. The aim of this study was to determine the effect of smoking habit on in vitro eicosanoid production by the intestinal mucosa in patients with IBD and controls.

Pinch biopsies from the colonic mucosa were obtained from 51 patients with IBD, of whom 9 were current smokers; and 95 patients in the control group, which contained 30 smokers. The biopsies were cultured for 48 hours at 37°C in a humified mixture of 5% CO_2 in air. Following culture PGE_2 and LTB_4 were measured in the biopsy tissue and in the culture medium by radioimmunoassay, and the total amount expressed per mg of protein in the biopsy (ng/mg protein).

Smoking had a biphasic effect on the eicosanoid production, in that light smokers (<10 cigarette per day) had enhanced PGE_2 and LTB_4 production (210.5 and 4.8 respectively); while medium smokers (10-19/day) had reduced production (27.6 and 3.7), which was enhanced in heavy smokers (>20/day), the difference reached significance (22.8 and 2.3) compared with non-smokers (44.3 and 4.2 $p<0.05$). The effects of smoking on eicosanoid production were more pronounced in patients with IBD, reaching significance in both light smokers (431.6 and 7.7 $p<0.05$) and heavy smokers (22.4 and 3.3 $p<0.05$) compared with non-smokers (59.4 and 4.8). The same trends were also seen in the control group, with light smokers producing more (54.4 and 4.8) and heavy smokers producing less (24.2 and 2.3) compared with non-smokers (28.8 and 4.0).

Cigarette smoking clearly has a profound effect on the aetiology of IBD, and the present study shows that heavy smoking inhibits eicosanoid production by the colonic mucosa, while light smokers may be exacerbating their condition by increasing their mucosal eicosanoid production.